

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

1 – 113. (Cancelled)

114. (Currently amended) An isolated protein that is free of all central nervous system myelin material ~~with which it is natively associated~~ comprising an amino acid sequence selected from the group consisting of

the polypeptide of SEQ ID NO: 2,

~~amino acids 975-1163 of SEQ ID NO: 2~~, and

amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2.

115. (Currently amended) An isolated protein that is free of all central nervous system myelin material ~~with which it is natively associated~~ comprising an amino acid sequence selected from the group consisting of

an amino acid sequence in which more than 90% of the amino acid residues in said sequence are identical to the amino acid residues of SEQ ID NO:2 in an alignment, and

an amino acid sequence in which more than 90% of the amino acid residues in said sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2,

wherein said protein has one or more Nogo functional activities activity selected from the group consisting of: (i) ability to bind to an antibody to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (ii) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (iii) ability to prevent regeneration of neurons in the spinal cord or brain; (iv) ability to confer to a substrate the property of restricting growth, spreading, and migration of neural cells; (v)

ability to inhibit dorsal root ganglia neurite outgrowth; (vi) ability to block NIH 3T3 cell spreading *in vitro*; and (vii) ability to block PC12 neurite outgrowth.

116. (Currently amended) An isolated protein that is free of all central nervous system myelin material ~~with which it is natively associated~~ comprising an amino acid sequence selected from the group consisting of

an amino sequence in which more than 95% of the amino acid residues in said sequence are identical to the amino acid residues of SEQ ID NO:2 in an alignment, and

an amino acid sequence in which more than 95% of the amino acid residues in said sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2,

wherein said protein has one or more Nogo functional activities activity selected from the group consisting of: (i) ability to bind to an antibody to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (ii) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:2 or consisting of amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2; (iii) ability to prevent regeneration of neurons in the spinal cord or brain; (iv) ability to confer to a substrate the property of restricting growth, spreading, and migration of neural cells; (v) ability to inhibit dorsal root ganglia neurite outgrowth; (vi) ability to block NIH 3T3 cell spreading *in vitro*; and (vii) ability to block PC12 neurite outgrowth.

117. (Currently amended) An isolated protein that is free of all central nervous system myelin material ~~with which it is natively associated~~ comprising an amino acid sequence selected from the group consisting of

the polypeptide of SEQ ID NO: 29,

~~the carboxy-terminal 188 amino acids of SEQ ID NO:29~~, and

amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO: 29.

118. (Currently amended) An isolated protein that is free of all central nervous system myelin material ~~with which it is natively associated~~ comprising

an amino sequence in which more than 90% of the amino acid residues in said sequence are identical to the amino acid residues of SEQ ID NO:29 in an alignment

wherein said protein has one or more Nogo functional activities activity selected from the group consisting of: (i) ability to bind to an antibody to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; (ii) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; (iii) ability to prevent regeneration of neurons in the spinal cord or brain; (iv) ability to confer to a substrate the property of restricting growth, spreading, and migration of neural cells; (v) ability to inhibit dorsal root ganglia neurite outgrowth; (vi) ability to block NIH 3T3 cell spreading *in vitro*; and (vii) ability to block PC12 neurite outgrowth.

119. (Currently amended) An isolated protein that is free of all central nervous system myelin material ~~with which it is natively associated~~ comprising

an amino sequence in which more than 95% of the amino acid residues in said sequence are identical to the amino acid residues of SEQ ID NO:29 in an alignment

wherein said protein has one or more Nogo functional activities activity selected from the group consisting of: (i) ability to bind to an antibody to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; (ii) ability to generate an antibody which binds to a protein consisting of SEQ ID NO:29 or consisting of amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO:29; (iii) ability to prevent regeneration of neurons in the spinal cord or brain; (iv) ability to confer to a substrate the property of restricting growth, spreading, and migration of neural cells; (v) ability to inhibit dorsal root ganglia neurite outgrowth; (vi) ability to block NIH 3T3 cell spreading *in vitro*; and (vii) ability to block PC12 neurite outgrowth.

120. to 122. (Cancelled)

123. (Currently amended) The protein of any one of claims 115, 116, 118, or 119, ~~or~~ 122, wherein said protein is mammalian.

124. (Currently amended) The protein of any one of claims 118, or 119, ~~or~~ 122, wherein said protein is human.

125. (Currently amended) The protein of any one of claims 114, 115, 116, 117, 118, or 119, ~~or~~ 120, ~~or~~ 122, wherein said protein is recombinant.

126. (Currently amended) An isolated nucleic acid comprising a polynucleotide which encodes ~~the protein of any one of claims 114, 115, 116, 117, 118, 119, 120, or 122, a protein comprising an amino acid sequence selected from the group consisting of~~

the polypeptide of SEQ ID NO: 2,

amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2,

the polypeptide of SEQ ID NO: 29, and

amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO: 29.

127. (Currently amended) An isolated nucleic acid comprising a polynucleotide which hybridizes to [[the]] a second nucleic acid which consists of a nucleotide coding sequence which encodes the amino acid sequence of SEQ ID NO: 2, amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2, SEQ ID NO: 29, or amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO: 29, of claim 126 under high stringency conditions comprising:

(a) hybridization in 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% of a copolymer of sucrose and epichlorohydrin FICOLL, 0.02% BSA, and 100 µg/ml denatured salmon sperm DNA at 65°C; and

(b) washing in a solution containing 2X SSC, 0.01% PVP, 0.01% of a copolymer of sucrose and epichlorohydrin FICOLL, and 0.01% BSA at 37°C for 1 h, and subsequently in 0.1X SSC at 50°C for 45 min;

wherein the polynucleotide encodes a protein that displays inhibitory activity in an NIH 3T3 fibroblast spreading assay.

128. (Currently amended) An expression vector comprising a nucleotide sequence which encodes ~~the protein of any one of claims 114, 115, 116, 117, 118, 119, 120, or 122. a protein comprising an amino acid sequence selected from the group consisting of~~

the polypeptide of SEQ ID NO: 2,

amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2,

the polypeptide of SEQ ID NO: 29, and

amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO: 29.

129. (Currently amended) An *ex vivo* recombinant host cell comprising the expression vector of claim ~~claims~~ 128.

130. (Previously presented) The *ex vivo* recombinant host cell of claim 129 wherein the recombinant host cell is a prokaryotic cell.

131. (Previously presented) The *ex vivo* recombinant host cell of claim 129 wherein the recombinant host cell is a eukaryotic cell.

132. (Currently amended) A method of producing a recombinant protein comprising culturing a recombinant host cell transformed with the nucleic acid of claim 126 such that [[a]] the protein encoded by said nucleic acid is expressed by said cell and recovering said expressed protein.

135. (Currently amended) An isolated ~~fragment of the protein of claim 115~~, wherein the protein fragment (a) is free of all central nervous system myelin material ~~with which the protein is natively associated~~; and (b) comprises

- (i) ~~an amino acid sequence consisting of amino acids 172 to 974 of SEQ ID NO:2;~~
- (ii) ~~an amino acid sequence consisting of amino acids 172 to 723 of SEQ ID NO:2;~~
- (iii) ~~an amino acid sequence consisting of amino acids 542 to 722 of SEQ ID NO:2;~~
- (iv) ~~an amino acid sequence consisting of amino acids 31-57 of SEQ ID NO:2;~~
- (v) ~~an amino acid sequence consisting of amino acids 11-191 depicted in Figure 14 (SEQ ID NO:32);~~
- (vi) ~~an amino acid sequence consisting of amino acids 988-1023 depicted in Figure 2a (SEQ ID NO:2);~~
- (vii) ~~an amino acid sequence consisting of amino acids 1090-1125 depicted in Figure 2a (SEQ ID NO:2);~~
- (viii) (i) ~~an amino acid sequence consisting of amino acids 623 to 640 of SEQ ID NO:2;~~
- (ix) (ii) ~~an amino acid sequence consisting of the amino acid sequence acids of SEQ ID NO:43;~~
- (x) (iii) ~~an amino acid sequence consisting of the amino acid sequence acids of SEQ ID NO:44;~~
- (xi) (iv) ~~an amino acid sequence consisting of the amino acid sequence acids of SEQ ID NO:45;~~
- (xii) (v) ~~an amino acid sequence consisting of the amino acid sequence acids of SEQ ID NO:46; or~~
- (xiii) ~~an amino acid sequence consisting of amino acids 1-171 of SEQ ID NO:2;~~
- (xiv) ~~an amino acid sequence consisting of amino acids 259-542 of SEQ ID NO:2;~~
- (xv) ~~an amino acid sequence consisting of amino acids 172-259 of SEQ ID NO:2;~~

- (xvi) an amino acid sequence consisting of amino acids 1-974 of SEQ ID NO:2;
- (xvii) an amino acid sequence consisting of amino acids 722-974 of SEQ ID NO:2;
- (xviii) an amino acid sequence consisting of amino acids 975-1162 of SEQ ID NO:2;

or

- (xix) (vi) an amino acid sequence consisting of amino acids 1-974 762-1163 of SEQ ID NO:2.

136. (Currently amended) An isolated ~~fragment of the protein of claim 115~~, wherein the protein fragment (a) is free of all central nervous system myelin material ~~with which the protein is natively associated~~; and (b) comprises consists of

(i) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 1-131 of SEQ ID NO:29;

(ii) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 132-939 of SEQ ID NO:29;

(iii) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 206-501 of SEQ ID NO:29;

(iv) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 501-680 of SEQ ID NO:29;

(v) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 132-206 of SEQ ID NO:29;

(vi) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 680-939 of SEQ ID NO:29; or

(vii) a first amino acid sequence in which more than 95% of the amino acid residues in said first sequence are identical to the amino acid residues of a second amino acid sequence in an alignment, said second amino acid sequence consisting of the amino acid sequence of amino acids 940-1127 of SEQ ID NO:29.

137. (Currently amended) An isolated ~~fragment of the protein of claim 115~~, wherein the protein fragment (a) is free of all central nervous system myelin material ~~with which the protein is natively associated~~; and (b) comprises

- (i) ~~an amino acid sequence consisting of amino acids 1-131 of SEQ ID NO:29;~~
- (ii) (i) an amino acid sequence consisting of amino acids 132-939 of SEQ ID NO:29;
- (iii) (ii) an amino acid sequence consisting of amino acids 206-501 of SEQ ID NO:29;
- (iv) (iii) an amino acid sequence consisting of amino acids 501-680 of SEQ ID NO:29; or
- (v) (iv) an amino acid sequence consisting of amino acids 132-206 of SEQ ID NO:29;
- ~~(vi) an amino acid sequence consisting of amino acids 680-939 of SEQ ID NO:29; or~~
- ~~(vii) an amino acid sequence consisting of amino acids 940-1127 of SEQ ID NO:29.~~

138. (New) An isolated nucleic acid comprising a polynucleotide which

- (i) hybridizes to a second polynucleotide under high stringency conditions comprising:
 - (a) hybridization in 6X SSC, 50 mM Tris-HCl (pH 7.5), 1 mM EDTA, 0.02% PVP, 0.02% of a copolymer of sucrose and epichlorohydrin, 0.02% BSA, and 100 µg/ml denatured salmon sperm DNA at 65°C; and

(b) washing in a solution containing 2X SSC, 0.01% PVP, 0.01% of a copolymer of sucrose and epichlorohydrin, and 0.01% BSA at 37°C for 1 h, and subsequently in 0.1X SSC at 50°C for 45 min;

wherein the second polynucleotide consists of a nucleotide coding sequence which encodes the amino acid sequence of SEQ ID NO: 2, amino acids 1-171 fused to amino acids 975-1163 of SEQ ID NO: 2, SEQ ID NO: 29, or amino acids 1-172 fused to the carboxy-terminal 188 amino acids of SEQ ID NO: 29; and

(ii) encodes a protein, wherein an antibody that binds to the protein also binds to a protein consisting of the amino acid sequence of SEQ ID NO:2 or SEQ ID NO:29.

139. (New) An isolated protein, wherein the protein (a) is free of all central nervous system myelin material; and (b) comprises:

(i) an amino acid sequence consisting of amino acids 31-57 of SEQ ID NO:2; or
(ii) an amino acid sequence consisting of amino acids 1090-1125 depicted in Figure 2a (SEQ ID NO:2).

140. (New) An isolated protein, wherein the protein (a) is free of all central nervous system myelin material; and (b) consists of:

(i) the carboxy-terminal 188 amino acids of SEQ ID NO:29;
(ii) an amino acid sequence consisting of amino acids 988-1023 of SEQ ID NO:2;
(iii) an amino acid sequence consisting of amino acids 975-1162 of SEQ ID NO:2;
(iv) an amino acid sequence consisting of amino acids 172 to 974 of SEQ ID NO:2;
(v) an amino acid sequence consisting of amino acids 172 to 723 of SEQ ID NO:2;
(vi) an amino acid sequence consisting of amino acids 542 to 722 of SEQ ID NO:2;
(vii) an amino acid sequence consisting of amino acids 1-171 of SEQ ID NO:2;
(viii) an amino acid sequence consisting of amino acids 1-974 of SEQ ID NO:2;
(ix) an amino acid sequence consisting of amino acids 1-131 of SEQ ID NO:29;
(x) an amino acid sequence consisting of amino acids 680-939 of SEQ ID NO:29;

- (xi) an amino acid sequence consisting of amino acids 940-1127 of SEQ ID NO:29;
- (xii) an amino acid sequence consisting of amino acids 259-542 of SEQ ID NO:2;
- (xiii) an amino acid sequence consisting of amino acids 172-259 of SEQ ID NO:2; or
- (xiv) an amino acid sequence consisting of amino acids 722-974 of SEQ ID NO:2.

141. (New) The protein of any one of claims 135, 136, and 137, wherein the protein is non-naturally occurring.